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Chromatographic purification of enveloped viruses

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Statement of the Problem: Mumps and measles virus are enveloped, RNA viruses that cause mumps and measles in humans, respectively. Mumps and measles virus particles are used in production of prophylactic vaccines and as gene vectors and oncolytic agents. Application of virus particles as biopharmaceutics requires highest purity to ensure potency and safety of the medicine. Impurities present in crude virus suspensions originate either from host cells (e.g. cellular DNA, exosomes), cultivation medium (e.g. BSA), from processing (e.g. extractables, leachables) or from the virus itself (e.g. aggregates, empty capsids).

Methodology & Theoretical Orientation: Due to the virus delicate macromolecular structure purification process needs to be powerful but gentle. Chromatography is gaining increasing interest in this regard especially due to development of monolithic columns. We have tested three modes of chromatography for purification of mumps and measles virus; ion-exchange, hydrophobic interaction, and affinity chromatography. Recovery of procedures was monitored by cell culture infectivity assay and measurement of total particle concentration using NanoSight. Host cell genomic DNA and proteins were measured using PCR and ELISA, respectively.

Results: Results showed that mumps and measles virus both bind strongly to anion exchange columns, but recovery of infective particles is below 20%. Immunoaffinity chromatography was performed using novel approach of elution with amino acids of high molarity at neutral pH. This approach was found effective for elution of functional virus particles and recoveries around 70% were obtained. Hydrophobic interaction chromatography was also successful with recoveries around 60%. Interestingly, recovery of infective virus particles in hydrophobic interaction chromatography was found to depend on the total-to-infective particle ratio in the starting crude virus suspension.

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